REMARKS/ARGUMENTS

I. Status of the Claims

Claims 1-21 are pending, with claims 3-21 withdrawn as directed to a non-elected invention. Upon entry of this amendment, claim 1 is amended and claims 2-21 canceled without prejudice or disclaimer. Claim 1 has been amended to focus on methods of current commercial interest, namely screening methods that identify potential immunosuppressants or potential modulators of B cell activation or tolerance.

New claims 22-35 are introduced upon entry of this amendment. These claims and amended claim 1 are supported throughout the specification including, for example, the following sections of the specification:

Claim 1:	page 18, line 21 to page 20, line 7; page 36, line 21 to page 37, line 6; and the examples.
Claims 22-23:	page 37, lines 7-8
Claim 24:	page 16, lines 2-11; and examples
Claims 25-26:	page 19, lines 1-10; and examples
Claims 27-28:	page 18, lines 21-34; and examples
Claims 29-30:	page 19, line 11 to page 20, line 7; and examples
Claims 31-32:	page 38, lines 11-24; page 43, line 14 to page 47, line 32.
Claims 33-35:	page 17, line 11

II. Claim Rejections under 35 U.S.C. 103(a)

Claims 1 and 2 are rejected as obvious over U.S. Patent No. 5,580,722 to Foulkes et al. ("Foulkes") over Cruse et al. (Illustrated Dictionary of Immunology; "Cruse"). Separately, these claims are also said to be obvious over published PCT application WO 97/10365 to Lockhart ("Lockhart") and U.S. Patent No. 6,110,666 to Grosveld ("Grosveld"). For the reasons that follow, it is submitted that the currently pending claims are not obvious over these combinations of references.

A. Currently Claimed Invention

Claim 1 has been amended to focus the claim on methods for screening drug candidates to identify a candidate that is a potential immunosuppressant or a potential modulator of B cell activation or B cell tolerance. This is possible because the current inventors have identified certain genes that are differentially expressed in different B cell states. The methods as presently claimed generally involve:

(1) providing a cell that expresses one or more of the expression profile genes that are recited in claim 1 (these are genes that are differentially expressed in various B cell states);

(2) adding a drug candidate to the cell;

(3) determining the expression level of the one or more expression profile genes in the cell;

(4) comparing the expression level of at least one gene of the one or more expression profile genes in the cell with the expression level of the at least one gene in a control cell not contacted with the agent; and

(5) identifying the drug candidate as a potential immunosuppressant or as a potential modulator of B cell activation or B cell tolerance if a difference in the expression level of the at least one gene is determined in the comparison step.

B. Foulkes and Cruse Distinguished

The Office Action states that Foulkes discusses methods for identifying compounds (e.g., drug candidates) that modulate the expression of certain genes that are associated with cardiovascular disease. It is acknowledged that Foulkes does not specifically discuss such screening methods with B cells. The Office Action states, however, that Foulkes lists CD36 as a potential protein of interest. Cruse is cited for the proposition that CD36 is expressed on B cells. It is thus concluded that it would be obvious to screen for compounds that affect the transcription of CD36 in B cells.

Foulkes and Cruse fail to render the current claims obvious, however, because, even when combined, these two references do not teach each and every element of claim 1 as required to establish a prima facie case of obviousness. These two references, for instance, do not teach or suggest a screening method involving comparing the expression level of at least one gene from those recited in claim 1 in a cell contacted with a drug candidate with the expression of the at least one gene in a control cell not exposed to the drug candidate. Nor do either of these references teach or suggest identifying the drug candidate as a potential immunosuppressant or as a potential modulator of B cell activation or B cell tolerance if a difference in the expression level of the at least one gene is determined during the comparison step.

In view of the shortcomings of these combined references, it is thus requested that this rejection be withdrawn.

B. Lockhart and Grosveld Distinguished

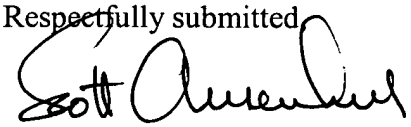
The Office Action is said to discuss methods for conducting array-based expression analysis, including detecting changes in expression due to exposure to drug candidates. Grosveld is said to discuss CD72 as a marker for pre-B cells. An entry for CD72 from the Illustrated Dictionary of Immunology is cited in support of the view that CD72 is a marker for B cells generally, not just pre-B cells. The combined references are thus said to render screening methods of B cells to monitor CD72 expression obvious.

Neither of these references, however, teach or suggest a method that involves both: (a) determining whether there is a difference in the expression level of at least one of the recited expression profile genes between a cell contacted with a drug candidate and a cell not contacted with the candidate agent, and (b) identifying a drug candidate for which a difference is determined as a potential immunosuppressant or a modulator of B cell activation or B cell tolerance. In fact, there is no discussion in either reference regarding B cell activation, tolerance or immunosuppression whatsoever. More specifically, there is no recognition that any of the expression profile genes are markers for B cell activation, tolerance of immunosuppression.

Because these two references, even when combined, also fail to teach or suggest each and every element of the present claims, it is thus requested that this ground of rejection also be withdrawn.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,



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